G3

detecting the presence of the microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exists.

Please add the following claim:

16. The system of claim 12 wherein the means for comparing comprises:

G4 a Raman detector in communication with a display.

REMARKS

Claims 2 and 9-15 have been rejected. Claims 9, 11 and 12 have been amended. Claim 16 has been added. No new matter has been added. Claims 2 and 9-16 remain for prosecution.

The Applicants do not know what requires correction other than the informality of the drawing and request clarification.

Claims 2 and 9-15 have been rejected pursuant to 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 2 and 9 have been amended to obviate the indefiniteness rejections.

Claims 12 and 14-15 have been rejected under 35 U.S.C. §102(b) as being anticipated by Nelson et al. (U.S. Pat. No. 4,847,198).

Applicants claim a system for the detecting the presence of a specific microorganism in a sample, the microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in the microorganism at a wavelength

between 242-257 nm that includes (a) means for contacting the sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on the microorganism to form an antigen-antibody complex, thereby immobilizing the microorganism on the solid phase, (b) means for irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy spectrum and (c) means for comparing the induced spectrum of step (b) with the characteristic spectrum to detect the presence of the microorganism in the sample. The system detecting the microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exists.

The limitations of claim 12 are set forth in means (or step) plus function language. That is, the limitations of claim 12 are expressed in language for performing a specified function without the recital of structure. See 35 U.S.C. §112, paragraph 6. Therefore, the limitation of claim 12 that recites, "means for contacting the sample with a medium comprising solid phase antibodies immobilized antibodies..." must be considered in its entirety. As Nelson et al. clearly does not disclose at the least the limitation of claim 12 that recites, "means for contacting the sample with a medium comprising solid phase immobilized antibodies...", it is respectfully requested that the anticipation rejection be withdrawn.

Claims 2, 9-10 have been rejected pursuant to 35 U.S.C. §103 as being obvious in view Nelson et al. (U.S. Pat. No. 4,487,198) and Tarcha et al. (U.S. Pat. No. 5,266,498).

Applicants claim a method for detecting the presence of a specific microorganism in a sample, the microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in the microorganism at a wavelength

between 242-257 nm, the method that includes (a) contacting the sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on the microorganism to form an antigen-antibody complex, thereby immobilizing the microorganism on the solid phase, (b) irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy and (c) comparing the induced spectrum of step (b) with said characteristic spectrum to detect the presence of the microorganism in the sample. The method detects the microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganism in the sample exists.

The Office Action contends that Nelson et al. teaches or suggests all the limitations of Applicants' claimed method except the limitation pertaining to contacting the sample with a medium comprising solid phase immobilized antibodies. The Office Action further contends that it would have been obvious to substitute the quartz plate disclosed in Nelson et al. with the solid phase immobilized antibodies disclosed in Tarcha et al. to produce Applicants' claimed method. See page 5, enumerated paragraph 6, bridging to pages 6-7 of the Office Action.

Tarcha et al. teaches a ligand binding assay for an analyte using surface enhanced Raman scattering wherein a complex that includes the analyte, an antibody having an affinity for the analyte, a Raman-active reporter and a particle having a metallic surface is formed and irradiated. The resultant resonance Raman spectra of the Raman-active reporter, enhanced by the metallic surface, is measured. See col. 5, lines 56-69, bridging to col. 6, lines 1-5 and col. 16, lines 1-20, in Tarcha et al.

Applicants submit that independent claim 2 is not obvious in view of Nelson et al. and Tarcha et al. because one of ordinary skill in the art would not have modified the Nelson et al. in view of Tarcha et al. to produce Applicants' claimed method with a reasonable degree of success. Tarcha et al. teaches the detection of an analyte in a sample by irradiating a complex that includes the analyte, an antibody having an affinity for the analyte, a Raman-active reporter and a particle having a metallic surface is formed and irradiated. In contrast to Applicants' claimed method which measures the resonance Raman spectra of the analyte, the method disclosed in Tarcha et al. measures the resonance enhanced Raman spectra of the Raman active reporter. What effect the substitution of the quartz plate disclosed in Nelson et al. with the immobilized antibodies disclosed in Tarcha et al. would have had on the resonance Raman spectra of an irradiated analyte/antibody complex and/or the detection thereof would have been purely speculative.

Further, Applicants' claimed method detects a microorganism, i.e. analyte, when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exists. Clearly, such a sensitive level of detection is not suggested by the combination of references, especially in view of the fact that Tarcha et al. is directed towards a method of detecting an analyte wherein the detection is based upon the resonance enhanced Raman spectra of a target molecule, i.e. the Raman active reporter, not the analyte. As the method for detection of the analyte disclosed in Tarcha et al. is distinct from the method disclosed in Nelson et al., Applicants also argues that the obviousness rejection is improperly based on hindsight reasoning.

In view of the foregoing, Applicants respectfully submit that the obviousness rejection of claim 9, and claims 2 and 10 dependent thereon, be withdrawn.

Claim 13 has been rejected under 35 U.S.C. §103 as being unpatentable in view of Nelson et al., Tarcha et al and Muller et al. (U.S. Pat. No. 5,126,244). Claim 13 is dependent on claim 9 which the Applicants believe is patentable and thus the dependent claims are also patentable.

Claims 2, and 9-10 are rejected under 35 U.S.C. §103(a) as being obvious in view of Chadha et al. in view of Tarcha et al.

The Office Action contends that Chadha et al. teaches or suggests all the limitations of Applicants' claimed method except the limitation pertaining to contacting the sample with a medium comprising solid phase immobilized antibodies. The Office Action further contends that it would have been obvious to substitute polysyline immobilization disclosed in Nelson et al. for site-specified immobilized antibodies disclosed in Tarcha et al. to produce Applicants' claimed method. See page 8, enumerated paragraph 8, bridging to page 9 of the Office Action. For the reasons discussed above in regard to Tarcha et al., Applicants submit that the obviousness rejection of claims 9 and claims 2 and 10 dependent thereon have been traversed.

Attached hereto is a marked-up version of the changes made to claims 9 and 12 by the current amendment. The attached page is captioned "**Version with markings to show changes made**".

It is respectfully submitted that the claims are now in condition for allowance and the same is earnestly solicited.

Respectfully submitted

Richard L. Stevens, Jr.
Registration No. 44,357
Samuels, Gauthier & Stevens
225 Franklin Street, Suite 3300
Boston, Massachusetts 02110
Telephone: (617) 426-9180
Extension 123

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 9 and 12 have been amended as follows:

Please amend the following claims:

9. (Quatro Amended) A method for detecting the presence of a specific microorganism in a sample, [said] the microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in [said] the microorganism[s] at a wavelength between 242-257 nm, the method comprising:

(a) contacting [said] the sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on [said] the microorganism to form an antigen-antibody complex, thereby immobilizing [said] the microorganism on [said] the solid phase;

(b) irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy[, said antibodies emitting essentially no resonance Raman spectra that interfere with the resonance Raman spectra of said microorganism]; and

(c) comparing [said] the induced spectrum of step (b) with [said] the characteristic spectrum to detect the presence of [said] the microorganism in [said] the sample[, the sample having at least 200 fold immobilized antibodies in excess of target antigen.], the method detecting the presence of the microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exists.

11. (Amended) The method of claim 9 wherein [said] the characteristic spectrum is at 1498 cm^{-1}.

12. (Thrice Amended) A system for [the] detecting the presence of a specific microorganism in a sample, [said] the microorganism having a characteristic resonance enhanced Raman backscattered energy spectrum produced by irradiating nucleic acids in [said] the microorganism[s] at a wavelength between 242-257 nm, the system comprising:

(a) means for contacting [said] the sample with a medium comprising solid phase immobilized antibodies which specifically bind to a characteristic cell surface antigen on [said] the microorganism to form an antigen-antibody complex, thereby immobilizing [said] the microorganism on [said] the solid phase[the solid phase antibodies being at least 200 fold in excess of antigen, the antibodies emitting essentially no resonance Raman spectra that interfere with the resonance Raman spectra of said microorganism when irradiated with a laser light of 242-257 nm];

(b) means for irradiating the solid phase of step (a) with a laser light of 242-257 nm to produce a resonance enhanced Raman backscattered energy spectrum; and

(c) means for comparing [said] the induced spectrum of step (b) with [said] the characteristic spectrum to detect the presence of [said] the microorganism in [said] the sample, the system detecting the presence of the microorganism when at least a 200:1 ratio of solid phase immobilized antibodies in the medium to microorganisms in the sample exists.